CHAPTER 5

DISCUSSION

The volunteers recruited into this study were from the fourth to the sixth year undergraduate dental students at the Faculty of Dentistry, Chiang Mai University. The age of the volunteers ranged between 21 to 25 years. There was no statistically significant difference of age between groups. Only healthy volunteers or American Society of Anesthesiologists (ASA) classification I, not taking medications and without contraindications for the use of N_2O/O_2 inhalation sedation were selected as subjects. Furthermore, the ratios of gender in each group were not different.

One hundred and twelve volunteers were randomized into four groups with different administrative and ending techniques. N_2O concentration required in each group ranged between 30-50% and there were no statistically significant differences of percentages of subjects required each concentration in each group. Eighty-four from 112 volunteers (75%) in this study required 50% N_2O to achieve the ideal stage of sedation and 50% N_2O was the concentration mostly required in all techniques. Approximately 20% of the subjects required 40% N_2O to achieve the ideal stage of sedation. Therefore, it can be concluded that majority of the subjects (95%) in this study required 40-50% of N_2O to get to the ideal stage of sedation. In contrast, many investigators recommended the proper concentration of N_2O for ideal sedation to be from 30-40% in their studies [1, 4, 5, 12, 75]. This minor difference maybe from the difference in criteria, study design or machine use. Becker and Rosenburg [6] stated

that the concentration of N_2O that actually reaches patients was reduced from the concentration delivered from the machine. Although 50% N_2O was the concentration mostly required in this study, the real concentration that volunteers received may be less than 50%.

In this study, the GA-VAS was used to assess anxiety level in volunteers prior to the N_2O/O_2 inhalation sedation. The pre-sedation anxiety level of the volunteers ranged between 0-82 mm. and there was no statistically significant difference between groups. However, the subjects in this study were healthy volunteers who did not have dental operation so pre-sedation anxiety level may be lower than anxiety level of patients who had dental operation.

The length of procedure in this study was between 16-25 minutes. There was statistically significant difference in the SO, RO groups and SR, RO groups. The slow titration (SO and SR) group had longer procedure time than the rapid induction (RO and RR) group with median of 18 minutes and 17 minutes respectively. The advantage of rapid induction technique was its ability to rapidly sedate patients thus they reach sedation level and get calmed quickly [(2)]. Surprisingly, there was the longest procedure time of 25 minutes in the RR group. This volunteer took a long time to reach the ideal stage of sedation although administered with the rapid induction technique. This event may be the result of the difference in individuals' biovariability as described by Clark and Brunick [(2)].

The main objective of this study was to assess the differences in the recovery period among different administrative and ending N_2O/O_2 sedation techniques. Several parameters were evaluated in this study. Physiologic parameters monitored in this study were blood pressure, heart rate and SaO_2. We monitored those parameters

of all groups in each step of sedation. Malamed [22] stated that there was no clinical significant effect on cardiovascular system when less than 80% of N_2O concentration was used. Similarly, Clark and Brunick [24] stated that effect of N_2O on the cardiovascular system did not produce any significant physiologic changes and some researchers reported only minor changes of blood pressure and heart rate from N_2O/O_2 inhalation sedation. Primosch et al. [75] studied physiologic parameters during 40% N_2O/O_2 inhalation sedation compared to 100% O_2 administration group and found heart rate reduction only in 40% N_2O/O_2 group. Clark and Brunick[24] explained that heart rate reduction from N_2O may be the result of patients' relaxation. In contrast, Leelataweewud et.al[76] reported that there was no statistically significant difference in pulse rate in the 50% N_2O/O_2 group combined with other sedative agents. In our study, there were no statistically significant differences in the change of blood pressure and heart rate from the baseline in each group at all time point recorded. Therefore, the different administrative and ending techniques did not significantly affect the change of blood pressure and heart rate in all steps of sedation.

No previous studies have ever directly monitored physiologic parameters at the end of procedure and during the recovery period. Although Jeske et al. in 2004 reported that there were no clinical significant changes in blood pressure, heart rate or respiratory rate in any subjects who were administered the slow titration technique with average concentration of N_2O at 35-40 % and ending with 100% O_2 or room air at anytime, they did not directly report on those physiologic parameters [12]. In our study, the change of systolic and diastolic blood pressure from the baseline of all sedation methods at each time point; pre-, during-, post-sedation and recovery period, were compared. There were statistically significant difference of systolic blood

pressure at the end of procedure between both groups ending with 100% O_2 (SO and RO group) and both groups beginning with rapid induction technique (RO and RR group). Similarly, there was statistically significant difference in change of heart rate from the baseline at the end of procedure in both groups beginning with rapid induction technique (RO and RR group). It is interesting that rapid induction technique may be shortly affect physiologic parameters at the end of procedure when ending either with 100% oxygen or room air. However, those physiologic parameters returned to close the baseline at the recovery period and there were no statistically significant difference at this period. Moreover, decrease of heart rate in every group in this study may result from volunteers' calm and relaxation from N_2O/O_2 inhalation sedation.

SaO_2 of arterial blood is the amount of O_2 that carried hemoglobin recorded by pulse oximeters. Normal SaO_2 at sea level is 95%, the level of SaO_2 was more decreased by the higher altitude [77]. Diffusion hypoxia is the phenomenon that is believed to occur because of decreased SaO_2 levels in blood rapidly following discontinuation of N_2O/O_2 without 100% O_2 administration. Application of 100% O_2 during the first 3-5 minutes following discontinuation of N_2O has been recommended to prevent diffusion hypoxia [1, 6, 9, 49, 50, 54]. Fink [49] in 1955 was the first describing diffusion hypoxia which was originally called diffusion anoxia demonstrating 8% drop in SaO_2 at the end of general anesthesia in 8 healthy patients who recovered in room air. The procedures were processed under general anesthesia through endotracheal tube with 75% N_2O/O_2 and 2.5% intravenous thiopental. Fanning and Colgan [54] in 1969 reported a large drop of SaO_2 after administration of 75% N_2O/O_2 and intravenous thiopental under general anesthesia in both animals and humans.

Moreover, Brodsky et al. [51] in 1988 recommended administering 100% O_2 to prevent hypoxemia in all patients although they found only 6% of clinically significant hypoxemia (SaO_2 < 90%) due to airway obstruction problems in those cases.

On the other hand, there were many studies that have questioned the necessity of administration of 100% O_2 to prevent diffusion hypoxia [4, 55, 56]. In dentistry, Quarnstrom et al. [11] studied diffusion hypoxia in 104 adult patients who were administered N_2O/O_2 by the slow titration technique with average concentration of N_2O at 35.5% and ending with room air. Result from this study showed that none of the cases had diffusion hypoxia. Similarly, study of Dunn-Russell et al. [4] that compared diffusion hypoxia between patients who recovered in room air or 100% O_2 after administered slow titration technique of N_2O revealed that SaO_2 recorded by pulse oximeter did not go below 95% in both groups. From that study, they concluded that there was no diffusion hypoxia when the patients were breathing room air instead of 100% O_2 after slow titration technique of N_2O. Moreover, there were no reports of diffusion hypoxia in the premixed 50% N_2O/O_2 which lacks the ability to administer 100% O_2 post -sedation [42].

In our study, diffusion hypoxia was evaluated from subjective symptoms and post-sedation SaO_2 drop compared to the baseline. The SaO_2 at baseline of all groups in this study was 99%. Leelataweewud et al. stated that true desaturation was a drop in SaO2 of 5% from baseline in a patient who was immobile and quiet[76]. Therefore, no clinical appearances of diffusion hypoxia together with less than 95% of SaO_2 were found in any groups in our study. Diffusion hypoxia occurred in the previous studies may be caused by the higher concentration of N_2O than that of the normal use in dental environment and also may be the result of other sedative agents use [11].

Similar to Becker's opinion, hypoxia only presented if high concentration (>70%) of N_2O/O_2 was used directly by full mask or endotracheal tube [6]. None of diffusion hypoxia occurred in our study may result from only the 30-50% N_2O/O_2 concentration was used via nasal hood without other anesthetic agents. Moreover, Leelataweewud stated that oxygen supplementation with N_2O in conscious sedation elevates the arterial oxygen tension (PaO_2) and O_2 in the functional residual capacity of the lung so desaturation in the apnea patients was delayed [76, 78]. However, only healthy volunteers were recruited in this study. The volunteers who had systemic diseases that were contraindications to the use of N_2O/O_2 sedation such as upper airway infections and inflammation, chronic obstructive pulmonary disease, acute respiratory infections were excluded. Therefore, major adverse events such as airway obstruction or apnea did not occur in this study.

Malamed [1] stated that 99% of the inspired N_2O were excreted within 5 minutes after N_2O cessation. Similarly, the report of diffusion hypoxia in Fink, Fanning and Colgan occurred during the first 4 minutes after N_2O termination [49, 54]. Dunn-Russell et al. recommended that SaO_2 should be monitored and recorded every 15 seconds for the 5 minutes after N_2O termination to detect significant diffusion hypoxia [4]. Although true diffusion hypoxia did not occur in our study, SaO_2 drop was detected since the first minute after N_2O termination in both groups ending with room air. There were statistically significant differences of SaO_2 drop at the fourth minute and the fifth minutes after N_2O termination between the same administrative groups and ending with 100% O_2 or room air (SO and SR group, RO and RR group). However, SaO_2 returned to the baseline within 0.50-3.50 minutes after the drop of SaO_2.

In the recovery period, Malamed [1] recommends the acceptable ranges of parameters as follows: blood pressure within ±20 mmHg/10 mmHg from the baseline, heart rate within ±15 beats/min from the baseline and respiratory rate within ±3 breaths/min. Similarly, Clark and Brunick [10] recommends that postoperative parameters should be blood pressure within 10 mmHg and heart rate within 10 beats/min from preoperative values. From our study, the range of change of blood pressure at recovery period was -3.61 to 0.14/-1.29 to 2.71 mmHg and the range of change of heart rate at recovery period was -5.82 to -0.50 beats/min from the baseline. The change of blood pressure and heart rate at the recovery period of our study were in the acceptable ranges similar to Malamed's recommendations although there were statistically significant differences in change of systolic blood pressure and heart rate from the baseline at the end of procedure mentioned earlier. Each volunteer was closely monitored for all physiologic parameters especially at the end of procedure and at the recovery period prior to patients' discharge.

Many authors investigated effects of N_2O on psychomotor ability, memory, and cognition and reported that psychomotor impairment may occur during N_2O/O_2 inhalation sedation [10, 37, 39, 64]. Therefore, psychomotor performance should be evaluated to confirm complete recovery prior to the patients' discharge. The Trieger test was used in this study. The median of time that psychomotor performance returned to the baseline was between 5-8 minutes after N_2O termination.

The Trieger test was first introduced by Dr. Norman Trieger in 1967 to evaluate psychomotor performance in the recovery period of patients who received IV sedation. Psychomotor impairment from the anesthetic drugs was reported in this study [62]. Then, Trieger et al. in 1971 used the Trieger test to evaluate psychomotor

performance after N_2O/O_2 sedation at 25, 50 and 70% concentration and reported that psychomotor impairment measured by the Trieger test could rapidly reverse to normal within 3-4 minutes after stopping N_2O/O_2 [64]. In 2004, Jeske et al. [12] used the Trieger test to assessed psychomotor performance at the recovery period in patients who obtained slow titration technique and completed with 100% O_2 or room air. No difference was found between both groups. However, they recorded errors only from dots that are missed at after 5 minutes in the recovery period compared to the baseline. Conry et al. [39] measured psychomotor changes by neuropsychological tests following 90 minutes of exposure to 20-35% N_2O/O_2 and 100% O_2 after completion. There were psychomotor impairment and this effect was delayed for 10 minutes after N_2O/O_2 was terminated. Therefore, recovery of psychomotor performance may relate to the length of procedure.

From this study, both dots that were missed completely and time to complete Trieger test were compared to the baseline. There were no signs of psychomotor impairment and no statistically significant difference was found between four groups. Therefore, different administrative and ending techniques of N_2O/O_2 inhalation sedation did not differently affect volunteers' psychomotor performances. None of psychomotor impairment occurred in this study may be from that only 30-50% N_2O/O_2 concentration without other anesthetic agent was used. Furthermore, the length of procedure in this study was short, between 16- 25 minutes. However, it is interesting that more errors on the Trieger test of some volunteers were related to symptoms of post-sedation complication at recovery period such as headache, confusion, lethargy and dizziness.

In this study, symptoms described as post-sedation complications were dizziness, headache, lethargy, confusion, nausea and vomiting. Dizziness was the most common complication occurred in all experimental groups. Fifty-three from 112 volunteers (47.32%) complained of dizziness and there were no statistically significant differences of dizziness between groups. From the previous study, dizziness was reported in different N_2O/O_2 administrative and ending techniques. In 1991, Quarnstrom et al. [11] reported 1.92% of dizziness in the slow titration technique with average concentration of N_2O at 35.5% and ending with room air. Moreover, the incidence of minor adverse effects including dizziness from the using of the premixed of 50% N_2O/O_2 were reported to be around 1-3% [42, 61, 79]. Thus, it may be assumed that the different N_2O administrative and ending techniques did not affect the occurrence of dizziness. The incidence of dizziness from this study was higher than the previous studies [11, 42, 79]. This difference may be from that some previous studies did not describe dizziness as post-sedation complication or explained this symptom with other words such as lightheadness or spinning [47, 57, 80]. Moreover, subjective symptoms in the recovery period were closely monitored in this study making the incidence of dizziness in this study higher than those of the previous studies. However, volunteers rapidly returned to their normal status within 30 minutes, the maximum time that dizziness disappeared, after N_2O/O_2 termination.

Nausea and vomiting were the most frequent complication reported in the previous studies [36, 47, 57]. From the retrospective study of Burnweit et al. [36] in 2004, there were 3% nausea and vomiting after 20-50% of N_2O administration by slow titration technique and ending with 100% O_2. Similarly, Kupietzky et al. [58] in 2008 reported less than 1% of post-sedation nausea and vomiting after rapid induction of

50% N_2O and ending with 100% O_2. From our study, nausea was found in 5.36% of the subjects and vomiting did not occur in all groups. Surprisingly, the highest frequency of nausea was found in the SO group and none was found in the SR group. However, there were no statistically significant differences of incidences of nausea between groups in this study.

The previous study stated that nausea and vomiting may be associated with oversedation, duration of sedation longer than 35 minutes, technique of N_2O/O_2 administration, patient's history of nausea and vomiting and the roller coaster effect which is the sharp increase and decrease concentration of N_2O/O_2 [6, 47, 58]. Moreover, Fisher [59] reported that postoperative nausea and vomiting may be affected from other anesthetic agents that combined with N_2O/O_2 such as cyclopropane or propofol. Kupietzky et al. [58] demonstrated that there was no difference of the incidence of nausea and vomiting between fasting and non- fasting group. Moreover, Malamed [47] stated that empty stomach may cause nausea and vomiting from starvation.

The volunteers in this study were instructed to have only light meal 2 hours before N_2O/O_2 administration as recommended by the AAPD [9]. The low incidence of nausea and vomiting in this study may be from many factors. First, the short duration of procedure that was only between 16-25 minutes was used in each sedation session. Second, the concentration of N_2O/O_2 was decreased when volunteers presented signs and symptoms of oversedation and appropriate concentration was maintained so the oversedation and roller coaster effect did not occur in this study. Third, only the N_2O/O_2 without other anesthetic agent was used in this study. In conclusion, there were no statistically significant differences of incidences of nausea

between groups so the different administrative and ending techniques did not related to the occurrence of nausea.

Oversedation may result in several minor complications such as headache, dizziness, nausea, confusion, and uncomfortable feeling in this study. Some volunteers had complained the symptoms of oversedation during the procedures so N_2O/O_2 concentration was decreased until symptoms of oversedation disappeared and the subjects returned to the ideal stage of sedation. It is interesting that when N_2O was terminated, some of those oversedation symptoms still presented in the recovery period. However, those symptoms totally returned to normal status within 30 minutes, the maximum time that oversedation symptoms disappeared after N_2O/O_2 termination.

Drowsiness and numbness were not reported as post-sedation complications in the previous studies [8, 36, 47, 61]. Clark and Brunick [8] stated that drowsiness was one of the symptoms of oversedation during N_2O/O_2 administration. Nevertheless, there were 16.96% of volunteers that complained of drowsiness in the recovery period in this study. Similarly, prolonged numbness on perioral soft tissue, feet and hands occurred approximately 6-8 % after N_2O termination. Although prolonged numbness on feet had the highest incidence (8%), perioral soft tissue numbness took a longer time to return to normal status than numbness in other areas. One volunteer in the RR group had prolonged perioral soft tissue numbness for 56 minutes after N_2O termination. However, there were no statistically significant differences of incidences of prolonged numbness in all groups.

When compared post-sedation complications between each experimental group, it is interesting that there were higher incidences of dizziness, drowsiness and nausea

in the slow titration technique than the rapid induction technique. Cumulative effect of N_2O/O_2 should be another factor to be considered. The depth of level of sedation may get deeper after long duration although the N_2O/O_2 concentration is not altered [(2)]. However, there were no statistically significant differences of post-sedation complications between all groups in this study.

Owing to its property, N_2O does not undergo biotransformation in the body; thus, it is completely eliminated through exhalation [(6)]. Malamed stated that the recovery time of N_2O/O_2 is very rapid because it is completely eliminated from the body within 3-5 minutes after N_2O discontinuation [(23)]. However, post-sedation complications such as lethargy, headache and nausea may occur in the recovery period. Clark and Brunick [(10)] recommended to give the patient post-oxygenation for 5 minutes to prevent these complications. Klein et al. [(81)] demonstrated that 30-195 seconds after N_2O termination were required by the patients who were sedated with 50% N_2O by rapid induction technique and ending with 100% O_2 to eliminate N_2O from their bodies. In our study, subjective symptoms disappeared after N_2O termination with the median range between 4.50 to 6.50 minutes. There was no statistically significant difference of subjective symptoms disappearance between groups.

Although subjective symptoms disappeared within 6.50 minutes, some of volunteers were not ready to be discharged. Therefore, complete recovery time from N_2O/O_2 sedation in this study was described as the time from N_2O termination until the volunteer was ready to go home. Takarada et al. [(48)] reported that the median recovery time of N_2O/O_2 inhalation sedation was 15 minutes in their study. Similarly, the mean recovery times of all groups in this study were between 16.18 to18.75 minutes. During recovery, subjective symptoms that the subjects complained were

prolonged numbness, dizziness, headache, lethargy, confusion and drowsiness as mentioned above. Although volunteers complained of subjective symptoms at the post-sedation stage in all groups, prolonged perioral soft tissue numbness from one volunteer in the RR group took the longest time (56 minutes) to disappear when compared to those of other groups. However, the significant difference in the complete recovery time was not found between groups. Therefore, we may assume from the results of our study that the recovery time was not affected by the different administrative and ending techniques of N_2O/O_2 inhalation sedation.

There was no previous study that compared volunteers' satisfactions from different N_2O/O_2 administrative and ending techniques. Although there were no statistically significant differences of satisfaction of sedation methods in this study, the highest level of satisfaction was in the SO group as expected. Moreover, the mean level of satisfaction of the groups that ending with 100% oxygen (SO and RO) were more than the groups that ending with room air (SR and RR). Therefore, it may be assumed that volunteers were more satisfied with the procedure ending with O_2. However, the subjects in this study were healthy volunteers who did not have dental operation. The satisfaction of N_2O/O_2 from patients who had dental operation may be different from their pre-sedation anxiety level and longer length of procedure.

Conclusion

This study demonstrated that the different administrative and ending techniques did not affect all clinical effects at recovery period and satisfaction of volunteers. Thus, the appropriate sedation method should be properly chosen for each patient. In cooperative patients, slow titration technique was recommended to prevent

oversedation. However, rapid induction technique or the premixed of 50% N_2O/O_2 were suitable for the uncooperative patients or emergency cases in order to reach sedation level quickly. Moreover, we challenged that the recommendation of recovery with 100% O_2 after N_2O/O_2 termination in all cases should be reconsidered. Although volunteers tended to be more satisfied with procedure ending with O_2, there were no statistically differences in clinical effects, psychomotor performance, recovery time and post-sedation complications between different ending techniques. Ending with 100% O_2 after less than 50% N_2O/O_2 sedation without other sedation agent may not be as critical as it was previously believed. Recovery with room air may be beneficial especially in the cases when patients vomit during procedure or patients have no desire to continue with N_2O/O_2 sedation**.**

Further research suggestions

Healthy adult volunteers without dental operation were selected in this study. However, other groups of samples such as pediatric patients and patients with operative plan should be considered for further research evaluation.